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Irreversible Electroporation: Disappearance of observable changes at imaging does not always imply complete reversibility of the underlying causal tissue changes

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Letter to editor

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3 **Irreversible Electroporation: Disappearance of observable changes at imaging does not**
4 **always imply complete reversibility of the underlying causal tissue changes**
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9 We read with great interest Padia et al. article emphasizing the potential role of early MR
10 assessment of irreversible electroporation (IRE) ablation in hepatocellular carcinoma (HCC)
11 patients (1). We especially appreciated that authors pointed out that IRE efficacy cannot be assessed
12 like for other physical ablative methods because cell death is no longer mainly related to thermal
13 coagulative necrosis (2). One singularity of the technique is that below 600V/cm the change in
14 permeability of cell membrane are assumed to be reversible (3). Thus, Padia et al. suggested that the
15 transient changes seen at the periphery of IRE ablation zone on the early MR examinations were
16 related to reversible effect of the treatment.
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21 From our point of view, this explanatory hypothesis calls some comments. The biological effects of
22 IRE on tissues are still unclear. Cell membrane electroporation leads to a swelling of the affected
23 cells as well as a release of cellular materials, which generate edema and inflammation in the tissue
24 (4). Such inflammation, visible with MRI disappears within few days (4, 5). On the other hand, it
25 has been reported that reversible electroporation lasts several tens of minutes and any way much
26 shorter than several hours (6). Interestingly, peripheral delayed enhanced zones have been also
27 described with perfusion CT performed immediately after IRE in livers of pigs (7).
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32 Histopathological analysis of livers harvested one day after showed a strong correlation between
33 these peripheral zones and red zones which contained hepatocytes involved in terminal apoptotic
34 process. Preliminary numerical simulations of IRE on tissue model showed also that the ablation
35 zone induced is wider than its central necrotic part (8). Indeed, IRE is a multiprobe ablative
36 technique requiring the placement of multiple electrodes into the tumor margin rather than in the
37 centre of the lesion(9). In this setting, we suggest that the disappearance of peripheral delayed
38 enhanced zones could be related to fast remodeling of apoptotic component of IRE ablation
39 combining resolution of inflammation, phagocytosis and replacement of dead cells, and not
40 necessarily to the recovery of basal membrane permeability of cells that were submitted to amount
41 of energy below irreversibility threshold.
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